

CORRECTED VERSION

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
28 April 2005 (28.04.2005)

PCT

(10) International Publication Number
WO 2005/038017 A3

(51) International Patent Classification⁷: **C12P 21/02**,
C12N 9/06, 15/53

(21) International Application Number:
PCT/US2004/031224

(22) International Filing Date:
23 September 2004 (23.09.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/505,807 25 September 2003 (25.09.2003) US

(71) Applicant (for all designated States except US): **MON-SANTO TECHNOLOGY LLC** [US/US]; 800 North Lindbergh Boulevard, St. Louis, MO 63167 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BOGOSIAN, Gregg** [US/US]; 374 Herworth Court, Clarkson Valley, MO 63005

(US). **O'NEIL, Julia, P.** [US/US]; 24 Hillard Road, Glen-dale, MO 63122 (US). **SMITH, Hong, Q.** [US/US]; 13501 Cedar Bridge Road, St. Louis, MO 63141 (US).

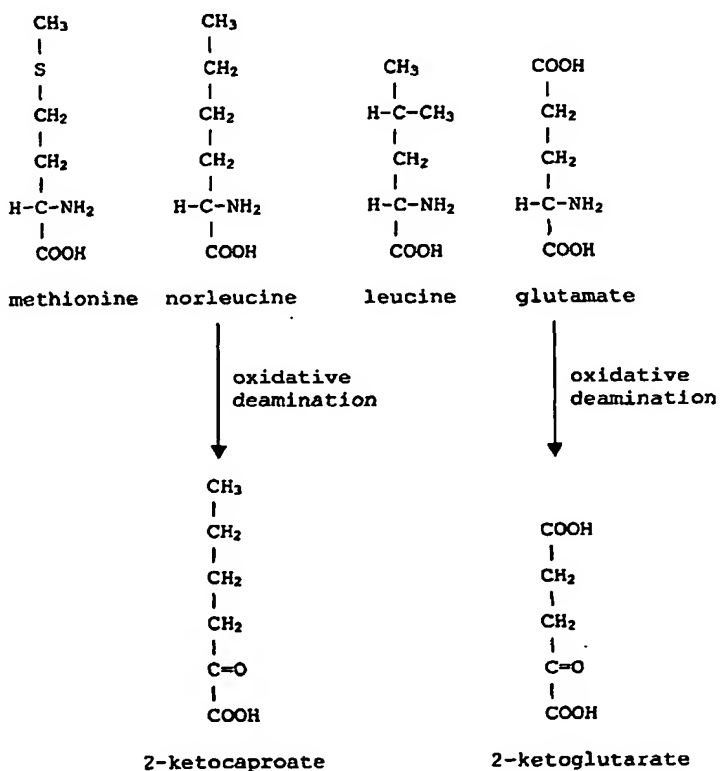
(74) Agent: **KAMMERER, Patricia, A.**; Howrey Simon Arnold & White, LLP, 2941 Fairview Park Drive Box 7, Falls Church, VA 22042 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH,

[Continued on next page]

(54) Title: PREVENTION OF INCORPORATION OF NON-STANDARD AMINO ACIDS INTO PROTEIN



(57) Abstract: The instant invention is drawn to the methods and compositions necessary to provide recombinant proteins with a substantially reduced or eliminated content of norleucine or other non-standard amino acids. Various embodiments of the invention provide for the substantial elimination of the incorporation of non-standard amino acids into recombinant proteins by the co-expression or enhanced expression of a protein (or the enzymatically active portion thereof) capable of degrading norleucine or other non-standard amino acids, including norvaline, beta-methylnorleucine, and homoisoleucine. In certain particular embodiments of the invention, the norleucine is degraded by a glutamate dehydrogenase, a leucine dehydrogenase, a valine dehydrogenase, a phenylalanine dehydrogenase, a glutamate/leucine/phenylalanine/valine dehydrogenase, or an opine dehydrogenase. Also provided are the cells and DNA constructs for carrying out these methods.



GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*

(88) Date of publication of the international search report:
11 August 2005

(48) Date of publication of this corrected version:

15 December 2005

(15) Information about Correction:

see PCT Gazette No. 50/2005 of 15 December 2005, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.